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| 09/801,925 | 03/09/2001 | Christa Hegele-Hartung | SCH-1754-P1 | 3436 |

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| EXAMINER | |
|---|---|
| QIAN, CELINE X | |
| **ART UNIT** | **PAPER NUMBER** |
| 1636 | 11 |

DATE MAILED: 01/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/801,925 | Applicant(s) HEGELE-HARTUNG ET AL. | |
|---|---|---|---|
| | Examiner Celine X Qian | Art Unit 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-26,28 and 29* is/are pending in the application.

4a) Of the above claim(s) *7-11,17-22,24 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-6,12-16,23,25,28 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

Claims 1-26, 28 and 29 are pending in the application. Claims 7-11, 17-22, 24 and 26 are withdrawn from consideration for being directed to non-elected subject matter. Claim 27 is cancelled.

This Office Action is in response to the Amendment filed on 11/18/02.

### *Response to Amendment*

The objection to claim 27 is moot in light of Applicants' cancellation of the claim.

The rejection of claims 1-6, 12-16, 23, 25, 28, 29 under 35 U.S.C. 112, first paragraph is maintained for reasons set forth of the record mailed on 6/7/02.

The rejection of claims 1-6, 12-16, 23, 25, 28, 29 under 35 U.S.C. 112, second paragraph is maintained for reasons set forth of the record mailed on 6/7/02.

### *Response to Arguments*

**Election/Restrictions**

In response to the restriction/election requirement, Applicants argue that the traversal should be accepted because not establish the search burden is a valid reason. This argument is accepted. However, Applicants fail to provide any reason to consider that the search burden has not been established by the previous office action mailed on 2/26/02. The inventions of Groups I-III are patentably distinct for reasons set forth of the record mailed on 4/1/02, and a search of all three groups within a single application is not co-extensive and is therefore burdensome. Therefore, the requirement is still deemed proper and therefore made final.

**Claim 28**

The Examiner acknowledges that claim 28 belongs to Group I and was considered in the previous office action. The Examiner apologizes for the confusion caused by misplacing this claim in the non-elected group. Claim 28, as the rest of the claims that belong to Group I, is rejected under 35 U.S.C. 112 first and second paragraph.

**The Claim Rejection under 35 USC 112, first paragraph**

In response to the 112 first paragraph, Applicants argue that the Examiner has provided no support for establishing that one of ordinary skill of art would doubt the objective truth of the asserted utility, which is established by the specification. Applicants further assert that the instant specification satisfies the requirements of enablement as applied to *In re Bundy*, which provided no example of specific compounds or specific use of any of the disclosed compounds. Applicants further argue that the claims specify a time, such as during post-ovulatory phase, and a dosage, 0.1-2 mg per subject for administration. Applicants further point out that the specification teaches a preferred mode on page 11, lines 14-19, lines 20 to page 12, line 8, and the dosage of the compound need not to be disclosed to satisfy the enablement requirement (cited *Cross v. Iizuka*). Applicants also argue that the Examiner's allegation that the demonstrated rabbit model does not correlate with an *in vivo* therapeutic activity is untenable for lack of support or reason. Applicants further argue that the law does not require that an Applicant to determine the behavior of claimed compounds in all imaginable ways. Moreover, Applicants assert that the parameters in determining the stage of endometrium maturation are not critical to the enablement of said method, and the results provided in Table 1 simply indicate that higher

doses of progesterone receptor antagonist 1 counteract the advancement of endometrium maturation associated with ovarian hyperstimulation, and low doses are effective in the methods.

These arguments have been considered but deemed not persuasive. First, the case law *In re Bundy* cannot be applied to the current situation to support the enablement of the present claims because it is applied to claims directed to chemical compounds. The current claims are directed to a method of inhibiting advanced endometrium maturation by administering a progesterone receptor antagonist. This method need to be enabled to its full scope based on analysis of factors include but not limited to (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the relative skill of those in the art; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue" (MPEP 2164.01 (a)). Such analysis was made in the previous office action and determines that the claims are not enabled based on the current specification.

Second, a preferred mode to practice the claimed method as taught by specification does not provide support to the full scope that is encompassed by the claims. The broadest claims encompass a method of inhibiting advanced endometrium maturation in any human or non-human female mammal undergoing fertility treatment by administering any 17α-fluoralkylated progesterone receptor antagonist of formula I at any time and at any amount. Although the law does not require the Applicant to determine the behavior of claimed compounds in all imaginable ways, the 35 USC 112 first paragraph does require the specification to describe the invention in such a way to enable one skilled in the art to practice the claimed method to its full scope

without undue experimentation. Again, the *Cross v. Iizuka* does not apply here because in that case, "the testimonial evidence of Dr. Ramwell, corroborated by certain documentary evidence, showed that those skilled in the art had available, at the critical date, information as to approximate dosage levels for the parent imidazole and 1-methylimidazole compounds to produce an I C50effect, i.e., a 50% inhibition of thromboxane synthetase, in a microsome milieu." In that situation, one skilled in the art can get the dosage level based on the relevant art to use the invention without undue experimentation. In the present claims, the broadest claim does not recite any effective amount to inhibit endometrium maturation in a human or a non-human mammal. Some claims do recite a effective range of 0.1-2 mg per subject on a single day. However, whether this amount is effective in all human or non-human mammal is unpredictable because of two reasons. A) In the example given on page 16, administering 1 mg progesterone receptor antagonist to the rabbit model apparently has given results that inclusive as to whether advanced endometrium maturation has been inhibited. The table shows that the uterine weight is decreased but uteroglobulin expression is very low. The specification states that higher doses of progesterone receptor antagonist counteracted the advancement of endometrium maturation, however, according to the uteroglobulin expression, it is not the case because the specification also discloses that low uteroglobulin expression indicate advanced endometrium maturation (see page 16, lines 8-10). B) The pharmacology of the claimed group of compounds including the rate of metabolism and half-life are different in mammals ranging from human to whale. As such, whether 0.1-2 mg is effective to inhibit advanced endometrium maturation is unpredictable.

Third, Applicants' assertion that the parameters in determining the stage of endometrium maturation are not critical is incorrect. It is unpredictable whether 1 mg and 10 mg are effective in inhibiting endometrium maturation of the rabbit model in the Example on page 16. Based on the uterine weight and Mc-Phail index, it appears that the endometrium maturation process is inhibited. However, based on uteroglobulin expression, the endometrium maturation is not inhibited. It appears that the result of these dosage is contradictory based on the above parameters. Therefore, choosing appropriate parameters is important in determining whether endometrium maturation is inhibited.

Fourth, the teaching of the specification appears to be contradictory. On page 11, the specification discloses that low doses of a progesterone receptor antagonist are effective in the claimed method. However, on page 16 (lines 8-10), the specification that higher doses of progesterone receptor antagonist counteracted the advancement of endometrium maturation. As such, it is unclear whether low dose or high dose is effective for the claimed method. In addition, it is unclear how to determine whether the dose is "high" or "low" in a particular mammal.

Lastly, Applicant appears to misconstrue the office action. The Examiner never implies that the demonstrated rabbit model does not correlate with an *in vivo* therapeutic activity. However, the a method of inhibiting endometrium maturation as broadly claimed is not enabled by this rabbit model described by the specification for the reasons set forth as the record mailed on 6/17/02 and discussed above. As such, the claims are not enabled by the instant specification. Therefore, this rejection is maintained.

**The Claim Rejection under 35 USC 112, second paragraph**

In response to the 112 second paragraph rejection, Applicants argue that the claims are directed to a method of inhibiting advanced endometrium maturation, and are not directed to a method for inhibiting and determining the result after the method was practiced. Applicants further argue that inhibition of advanced endometrium maturation occurs regardless of whether one determines if it occurred, thus the step to determine whether endometrium maturation is inhibited is not an essential step.

This argument has been considered but deemed not persuasive. The method steps of the claim are in conflict with the preamble of the claim. The preamble recites a method of inhibiting endometrium maturation. However, the method steps does not come back to this statement. No inhibition is achieved. Therefore, this rejection is maintained.

***Conclusion***

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.
January 27, 2003

Anne-Marie Falk
ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER